Fast and slow rates of symptom progression in the transgenic SOD1 murine model of ALS

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Abstract

ALS is a disease targeting motoneurons (MN). In the SOD1 mouse model of ALS, an axonal die-back process is initiated during the pre-symptomatic stage where MN axons withdraw from target muscle. We have used facial nerve axotomy, which resembles the axonal die-back response, in pre-symptomatic SOD1 mice to investigate aspects of the disease. Apoptotic and pro-inflammatory gene expression is upregulated in pre-symptomatic SOD1 axotomized facial nuclei in addition to significant SOD1 MN death. Disease progression in symptomatic SOD1 facial nuclei resembles the molecular response initiated by axotomy. MN survival levels in symptomatic SOD1 and axotomized, presymptomatic SOD1 facial nuclei are similar. Therefore, facial nerve axotomy produces a disease onset-like response. The current study used behavioral testing to assess motor function, and revealed two groups of SOD1 mice with differing rates of symptomatic disease progression. The slow progression group had significantly less motor impairments compared to the fast progression group, but no difference in symptom onset was seen. Fast progression group showed higher mRNA levels for genes related to axonal injury. Symptomatic severity in SOD1 mice correlates to the cellular and molecular responses to axonal injury. Therefore, research using treatments to slow disease or extend